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Substitute	for form 1449A/F	то		Complete If Known			
	_ \.			Application Number	09/713,920 10/603.036		
INFO	RMATIO	n discl	.OSURE	Filing Date	November 15, 2000 July 18 2003		
STAT	TEMENT	BY APP	LICANT	First Named Inventor	Stemmer		
				Art Unit	1648 /637		
	(use as many s	sheets as nec	essary)	Examiner Name	Park, H. Jamuel Woolwine		
Sheet	1	of	17	Attorney Docket Number	018097-032500US-C100. 327US		

			U.S. PATENT D	OCUMENTS	
		Document Number			
Examiner	Cite No.1	Number Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
/S.W./	AA	US-6,365,408	04-02-2002	Stemmer	
	ΑB	US-6,361,974	03-26-2002	Short et al.	
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	AD	US-6,352,842	03-05-2002	Short et al.	
	AE	US-6,323,030	11-27-2001	Stemmer	
	AF	US-6,297,053	10-02-2001	Stemmer	Cos,
	AG	US-6,291,242	09-18-2001	Stemmer	<i>∞</i> ,
	AH	US-6,287,861	09-11-2002	Stemmer et al.	
	AI	US-6,277,638	08-21-2001	Stemmer	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
	AJ	US-6,180,406	01-30-2001	Stemmer	
	AK	US-6,174,673	01-16-2001	Stemmer	The state of the s
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	AQ	US-6,096,548	08-01-2000	Stemmer	
	AR	US-6,093,873	07-25-2000	Chambon et al.	
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	AV	US-6,071,889	06-06-2000	Weiss et al.	
	AW	US-6,057,103	05-02-2000	Short	·
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	AY	US-6,051,409	04-18-2000	Hansen et al.	
	AZ	US-6,030,779	02-29-2000	Short	· · · · · · · · · · · · · · · · · · ·
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Λ	BJ	US-5,877,402	03-02-1999	Maliga et al.	

Examiner Signature	/Samuel Woolwine/	Date Considered	05/01/2007
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Substitute f	or form 1449A/F	то		Complete If Known			
				Application Number	09/713,920 10/6 23 03 6		
INFO	RMATIO	n discl	.OSURE	Filing Date	November 15, 2000 7//3/03		
STATEMENT BY APPLICANT				First Named Inventor	Stemmer		
				Art Unit	1648 1637		
(use as many s	sheets as nec	essary)	Examiner Name	Park, H. Jamuel Woolwine		
Sheet	2	of	17	Attorney Docket Number	018097-032500US 0/00. ススフルタ		

			U.S. PATENT D	OCUMENTS	
		Document Number			
Examiner	Cite No.1	Number Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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	BL	US-5,866,363	02-02-1999	Pieczenik	
	BM	US-5,858,725	01-12-1999	Crowe et al.	
	BN	US-5,851,813	12-22-1998	Desrosiers	
	ВО	US-5,843,643	12-01-1998	Ratner	
	BP	US-5,837,458	11-17-1998	Minshull et al.	
	BQ	US-5,834,252	11-10-1998	Stemmer et al.	
	BR	US-5,830,721	11-03-1998	Stemmer et al.	<u>C</u>
	BS	US-5,830,696	11-03-1998	Short	Cos
	вт	US-5,824,514	10-20-1998	Kauffman et al.	
	BU	US-5,824,485	10-20-1998	Thompson et al.	PON PAREN
	BV	US-5,824,469	10-20-1998	Horwitz et al.	'On
	BW	US-5,817,483	10-06-1998	Kauffman et al.	70
	BX	US-5,814,476	09-29-1998	Kauffman et al.	A_{\wedge}
	BY	US-5,811,238	09-22-1998	Stemmer et al.	'7 <u>^</u>
	BZ	US-5,808,022	09-15-1998	Huse	\sim
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	CB	US-5,783,431	07-21-1998	Peterson et al.	
	CC	US-5,773,267	06-30-1998	Jacobs et al.	
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	CF	US-5,756,316	05-26-1998	Schellenberger	
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	CL	US-5,629,179	05-13-1997	Mierendorf et al.	
	CM	US-5,605,793	02-25-1997	Stemmer -	
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	CO	US-5,556,772	09-17-1996	Sorge et al.	
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	CQ	US-5,541,309	06-30-1996	Prasher	
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V	СТ	US-5,514,568	05-07-1996	Stemmer	

Signature /Samuel Woolwine/ Considered 05/01/2007	Examiner Signature	/Samuel Woolwine/		05/01/2007	
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¹ Applicant's unique citation designation number (optional). ² Kind Codes of U.S. Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. Applicant is to place a check mark here if English language Translation is attached.

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Substitute	for form 1449A/PTO			Complete if Known			
INFORMATION DISCLOSURE				Application Number	-09/713,920 10/6d3,036		
				Filing Date	November 15, 2000 1/19/03		
STAT	STATEMENT BY APPLICANT		First Named Inventor	Stemmer			
			Art Unit	1648 /63/			
(use as many sheets as necessary)		Examiner Name	Park, H. Jamuel Woolwine				
Sheet	3	of	17	Attorney Docket Number	04007-039500US () 1(1)) 7 71, S		

			U.S. PATENT D	OCUMENTS	
		Document Number			T
Examiner	Cite No. ¹	Number Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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	CW	US-5,489,523	02-06-1996	Mathur	
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	DG	US-5,234,824	08-10-1993	Mullis	
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	DO	US-5,023,171	06-11-1991	Ho et al.	
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Examiner Signature	/Samuel Woolwine/	Date Considered	05/01/2007

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Substitute for form 1449A/PTO Complete if Known Application Number 09/713,920 10/623 036 INFORMATION DISCLOSURE Filing Date November 15, 2000 STATEMENT BY APPLICANT First Named Inventor Stemmer **Art Unit** 1648 (use as many sheets as necessary) Examiner Name Park-H. ى Samue Sheet of 17 018097-032500US O/OO. 22765 Attorney Docket Number

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/S.W./	DW	EP	252 666	12-16-1998			
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	DY	EP	552 266	01-19-2000			
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	EG	WO ·	90/14424	11-29-1990	-	PONT PARENT	
	EH	WO	90/14430	11-29-1990		Ø_	
	EI	wo	91/01087	02-07-1991		10/1	
	EJ	wo	91/06570	05-16-1991	· · · · · · · · · · · · · · · · · · ·	1/1/	
	EK	wo	91/06643	05-16-1991	•	A.	Ē
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1	EM	wo	91/07506	05-30-1991			Ī
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	EO	wo	91/16427	10-31-1991			
	EP	wo	92/06176	04-16-1992	· · · · · · · · · · · · · · · · · · ·		
	EQ	wo	92/07075	04-30-1992			Ē
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	ES	wo	93/01282	01-21-1993			
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1	EX	wo	93/15208	08-05-1993			
	EY	wo	93/16192	08-19-1993			
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	FA	wo	93/19172	09-30-1993			
	FB	wo	93/25237	12-23-1993			Ē
	FC	wo	94/03596	02-17-1994			
	FD	wo	94/09817	05-11-1994			Ħ
	FE	wo	94/11496	05-26-1994			1
V	FF	wo	94/13804	06-23-1994			Ī

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Substitute for form 1449A/PTO Complete if Known **Application Number** 10/623036 09/713,920 INFORMATION DISCLOSURE Filing Date November 15, 2000 STATEMENT BY APPLICANT **First Named Inventor** Stemmer Art Unit 1648 (use as many sheets as necessary) **Examiner Name** Park, H. Jomuel C. Woolwine Sheet 5 17 Attorney Docket Number 018097-032500US 0100 22745

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Examiner Initials*	Cite No.1	For	reign Patent Docur		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	1
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Substitute	for form 1449B/P	то			Complete if Known,
INEO	DAAATIOI	N DICCI	OCUPE	Application Number	09/713,920 10/623036
	RMATIO			Filing Date	Nevember 15, 2000 7/19/03
SIAI	EMENT	BY APP	LICANT	First Named Inventor	Stemmer
				Art Unit	1848 /637
	(use as many s	heets as ned	essary)	Examiner Name	Park, H. Samuel Woolwine
Sheet	6	of	17	Attorney Docket Number	-018097-032500US 0100. 221

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.1	include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Т
/S.W./	GC	Adey et al., "Preparation of second-generation phage libraries," Phage Disp. Pept. Proteins, eds. Kay et al., pgs. 277-291 (1996).	
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	Gì	Bartel et al., "Isolation of New Ribozymes From a Large Pool of Random Sequences", Science, 261:1411-1418 (1993)	
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	GO	Cadwell et al., "Randomization of Genes by PCR Mutagenesis," PCR Methods and Applications, 2:28-33 (1992).	
V	GP	Calogero et al., "In Vivo Recombination and the Production of Hybrid Genes," Microbiology Letters, 76:41-44 (1992).	

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Examiner Signature	/Samuel Woolwine/	Date Considered	05/01/2007	. •

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	Substitute fo	or form 1449B/F	PTO		·	Complete if Known
	INFOR	INFORMATION DISCLOSURE		Application Number	09/713,920 10/693,036	
					Filing Date	November 15, 2000- 7/13/03
	STATI	EMENT	BY APP	LICANT	First Named Inventor	Stemmer
					Art Unit	1648 /637
	(use as many sheets as necessary)				Examiner Name	Park, H. Samuel Woolwing
く	Sheet 7 of 17				Attorney Docket Number	1018097-032500US-DICO. J27US

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Т
/S.W./	GQ	Carneron et al., "Cellular and Metabolic Engineering An Overview", Applied Biochem, Biotech., 38: 105-140 (1993).	
	GR	Caren et al., "Efficient Sampling of Protein Sequence Space for Multiple Mutants," <u>Biotechnology</u> , 12(5):517-520 (1994).	
	GS	Carter, P., "Improved Oligonucleotide-Directed Mutagenesis Using M13 Vectors," Methods in Enzymology, 154:382-383 (1985).	
	GT	Chakrabarty, "Microbial Degradation of Toxic Chemicals: Evolutionary Insights and Practical Considerations", ASM News, 62(3): 130-137 (1996).	
	GU	Chater, "The Improving Prospects for Yield Increase by Genetic Engineering in Antibiotic-Producing Streptomycetes", <u>Biotechnology</u> , 8: 115-121 (February 1990).	
	σv	Chen et al., "Tuning the activity of an enzyme for unusual environments: Sequential random mutagenesis of subtilisin E for catalysis in dimethylformamide", PNAS, 90: 5618-5622 (June 1993).	
	GW	Clackson et al., "Making antibody fragments using phage display libraries," Nature, 352:624-628 (August 15, 1991).	
	GX	Collet et al., "A Binary plasmid System for shuffling combinatorial antibody Libraries," PNAS, 89(21):10026-10030 (1992).	
	GY	Crameri et al., "Combinatorial Multiple Cassette Mutagenesis Creates All The Permutations Of Mutant And Wild-Type Sequences", <u>Biotechniques</u> , 18(2):194-196 (1995)	
	GZ	Crameri et al., "Improved Green Fluorescent Protein By Molecular Evolution Using DNA Shuffling", Nat. Biotechnol., 14(3):315-319 (1996)	
	НА	Crameri et al., "Construction And Evolution Of Antibody-Phage Libraries By DNA Shuffling", Nat. Med., 2(1):100-102 (1996)	
	НВ	Crameri et al., "Molecular Evolution Of An Arsenate Detoxification Pathway By DNA Shuffling", Nat. Biotechnol., 15(5):436-438 (1997)	
	нс	Crameri et al., "DNA Shuffling Of A Family Of Genes From Diverse Species Accelerates Directed Evolution", Nature, 391(3664):288-291 (1998)	
$\overline{\mathbf{V}}$	HD	Crameri et al., "10(20)-Fold aptamer library amplification without gel purification," Nuc. Acids Res., 21(18):4410 (1993).	

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Examiner Signature	/Samuel Woolwine/	Date Considered	05/01/2007	

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Substitute for	form 1449B/P	то			Complete if Known
INFOR	RAATIOI	N DIOO!	OCUPE	Application Number	09/713,920 10/623,036
			OSURE	Filing Date	November 15, 2000 7/18/03
STATE	MENT	BY APP	LICANT	First Named Inventor	Stemmer
				Art Unit	1648 1637
(us	se as many s	sheets as nec	essary)	Examiner Name	Rark, H. Samuel Woolwine
Sheet	8	of	17	Attorney Docket Number	018097-032500US 0100. da745

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the Item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Т
/S.W./	HE	Cull et al., "Screening for receptor ligands using large libraries of peptides linked to the C terminus of the lac repressor," PNAS, 89:1865-1869 (March 1992).	
	HF	Cwirla et al., "Peptides on phage: A vast library of peptides for identifying ligands," PNAS, 87:6378-6382 (August 1990).	
	HG	Daugherty et al., "Polymerase chain reaction facilitates the cloning, CDR-grafting, and rapid expression of a murine monoclonal antibody directed against the CD18 component of leukocyte integrins," Nuc. Acids Res., 19(9):2471-2476 (1991).	
	нн	Delagrave et al., "Recursive Ensemble Mutagenesis," <u>Protein Engineering</u> , 6(3):327-331 (1993).	
	ні	Delagrave et al., "Searching Sequence Space to Engineer Proteins: Exponential Ensemble Mutagenesis," <u>Biotechnology</u> , 11:1548-1552 (December 1993).	
	HJ	Dieffenbach et al., PCR Primer, A Laboratory Manual, Cold Spring Harbor Laboratory Press, pgs. 583-589, 591-601, 603-612, and 613-621 (1995).	
	нк	Dube et al., "Artificial mutants Generated by the Insertion of Random Oligonucleotides into the Putative Nucleoside Binding Site of the HSV-1 Thymidine Kinase Gene," <u>Biochemistry</u> , 30(51):11760-11767 (1991).	
	HL	Evnin et al., "Substrate specificity of trypsin investigated by using a genetic selection", <u>PNAS</u> , 87: 6659-6663 (September 1990).	
	НМ	Fang et al., "Human Strand-specific Mismatch Repair Occurs by a Bidirectional Mechanism Similar to That of the Bacterial Reaction", J. Biol. Chem., 268(16): 11838-11844 (June 5, 1993).	
	HN	Feinberg et al., "A Technique for Radiolabeling DNA Restriction Endonuclease Fragments to High Specific Activity," Anal. Biochem., 132:6-13 (1983).	
	НО	Fisch et al., "A Strategy Of Exon Shuffling For Making Large Peptide Repertoires Displayed On Filamentous Bacteriophage", Proc Natl Acad Sci USA, 93(15):7761-7766 (1996)	
	HP	Fullen et al., "Genetic Algorithms and Recursive Ensemble Mutagenesis in Protein Engineering," Complexity Int.'1 1994 I, printed from website http://www.csu.edu.au/ci/vol1/fuellen/REM.html on 12/7/99.	
	НQ	Gates et al., "Affinity Selective Isolation Of Ligands From Peptide Libraries Through Display On A Lac Repressor 'Headpiece Dimer'", J. Mol. Biol., 255(3):373-386 (1996)	
V	HR	Ghosh et al., "Arginine-395 Is Required for Efficient in Vivo and in Vitro Aminoacylation of tRNAs by Escherichia coli Methionyl-tRNA Smthetase," Biochemistry, 30:11767-11774 (1991).	

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Substitute for form 1449B/PTO Complete if Known Application Number 09/713,920 /0/ 623 INFORMATION DISCLOSURE Filing Date November 15, 2000 4/ STATEMENT BY APPLICANT First Named Inventor Stemmer 1637 Art Unit 1048 (use as many sheets as necessary) **Examiner Name** Park; H. Junuel Sheet of Attorney Docket Number

Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
/S.W./	HS	Goldman et al., "An Algorithmically Optimized Combinatorial Library Screened by digital Imaging Spectroscopy," <u>Biotechnology</u> , 10:1557-1561 (December 1992).	
	нт	Graf et al., "Random circular permutation of genes and expressed polypeptide chains: Application of the method to the catalytic chains of asparate transcarbamoylase," PNAS, 93:11591-11596 (1996).	
	HU	Gram et al., "In Vitro Selection and Affinity Maturation of Antibodies From a Naïve Combinatorial Immunoglobulin Library", Proc. Natl. Acad. Sci. USA, 89:3576-3580 (1992)	
	HV	Greener et al., "An Efficient Random Mutagenesis Technique Using An E. coli Mutator Strain", Methods in Molecular Biology, 57:375-385 (1995)	
	HW	Harlow et al., "Construction of Linker-Scanning Mutations using the Polymerase Chain Reaction," Methods in Mol. Biol., 31:87-96 (1994).	
	нх	Heda et al., "A simple <i>in vitro</i> site directed mutagenesis of concatamerized cDNA by inverse polymerase chain reaction," Nuc. Acids Res., 20(19):5241-5242 (1992).	
	НҮ	Heim et al., "Wavelength Mutations And Posttranslational Autoxidation Of Green Fluorescent Protein", Proc. Natl. Acad. Sci. USA, 91(26):12501-12504 (1994)	
	HZ	Hermes et al., "Searching Sequence Space by Definably Random Mutagenesis: Improving the Catalytic Potency of an Enzyme," Proc. Natl. Acad. Sci. USA, 87(2):696-700 (1990).	
	IA	Higuchi et al., "A general method of in vitro preparation and specific mutagenesis of DNA fragments: study of protein and DNA interactions," Nuc. Acids Res., 16(15):7351-7367 (1988).	
	IΒ	Ho et al., "DNA and Protein Engineering Using the Polymerase Chain Reaction: Splicing by Overlap Extension," DNA and Protein Eng. Techniques, 2(2):50-55 (1990).	
	IC	Ho et al., "Site-Directed Mutagenesis by Overlap Extension Using the Polymerase Chain Reaction," Gene, 77:51-59 (1989).	
	ID	Hodgson, "The Whys and Wherefores of DNA Amplification," Biotechnology, 11:940-942 (August 1993).	
	IE	Horton et al., "Gene Splicing by Overlap Extension," Mehtods in Enzymology, 217:270-279 (1993).	
$\overline{\mathbf{V}}$	IF	Horton et al., "Gene Splicing by Overlap Extension: Tailor-Made Genes Using the Polymerase chain Reaction," BioTechniques, 8(5):528-535 (May 1990).	

Signature /Samuel Woolwine/ Considered 05/01/2007	Examiner Signature	/Samuel Woolwine/	Date Considered	05/01/2007
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				Art Unit	1648 /637
(us	se as many sh	eets as ne	cessary)	Examiner Name	Park, H. Samuel Woolwine
Sheet	10	of	17	Attorney Docket Number	018097-032500USO/00. 227US

			OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Exam Initial		Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
/\$	S.W./	IG	Horton et al., "Engineering Hybrid Genes Without the Use of Restriction Enzymes: Gene Splicing by Overlap Extension," Gene, 77:61-68 (1989).	
		IH	Ippolito et al., "Structure assisted redesign of a protein-zinc-binding site with femtomolar affinity", PNAS, 92: 5017-5021 (May 1995).	
		11	Janczewski et al., "Molecular phylogenetic inference from saber-toothed cat fossils of Rancho La Brea," PNAS, 89:9769-9773 (1992).	
		n.	Jayaraman et al., "Polymerase chain reaction-mediated gene synthesis: Synthesis of a gene coding for isozyme c of horseradish peroxidase," PNAS, 88:4084-4088 (May 1991).	
		ΙK	Jones et al., "A Rapid Method for Recombination and Site-Specific Mutagenesis by Placing Homologous ends on DNA Using Polymerase Chain Reaction," <u>BioTechniques</u> , 10(1): 62-66 (1991).	
		IL	Jones et al., "Recombinant Circle PCR and Recombination PCR for Site-Specific Mutagenesis Without PCR Product Purification," Biotechniques 12(4):528-534 (1992).	
		IM	Joyce, G. F., "Directed Molecular Evolution," Scientific American, (December 1992).	
		IN	Kang et al., "Antibody redesign by chain shuffling from random combinatorial immunoglobulin libraries," PNAS, 88(24):11120-11123 (1991).	
		Ю	Kellogg et al., "Plasmid-Assisted Molecular Breeding: New Technique for Enhanced Biodegradation of Persistent Toxic Chemicals", Science, 214: 1133-1135 (December 4, 1981).	
		IP	Kim et al., "Cloning and Nucleotide Sequence of the Collb Shufflon," Plasmid, 22:180-184 (1989).	
		IQ	Kim et al., "Human Immunodeficiency Virus Reverse Transcriptase," The Journal of Biological Chemistry, 271(9):4872-4878 (1996).	
		IR	Klug et al., "Creating chimeric molecules by PCR directed homologous DNA recombination," Nuc. Acids Res., 19(10):2793 (1991).	
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1	/	ΙΤ	Komano et al., "Distribution of Shufflon among Incl Plasmids," J. Bacteriology, 169(11):5317-5319 (1987).	

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Examiner Signature	/Samuel Woolwine/	Date Considered	05/01/2007

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Substitute for form 1449B/PTO	Complete if Known		
INFORMATION PLOOP COURT	Application Number	09/713,920 10/6:33 036	
INFORMATION DISCLOSURE	Filing Date	Nevember 15, 2000 7/13/03	
STATEMENT BY APPLICANT	First Named Inventor	Stemmer	
	Art Unit	1648 /637	
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Sheet 11 of 17	Attorney Docket Number	018097-032500US 0100. 237US	

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/S.W./	īU	Kramer et al., "Oligonucleotide-directed construction of mutations via gapped duplex DNA," Methods in Enzymology, 154:350-367 (1987).	
	ΓV	Krishnan et al., "Direct and crossover PCR amplification to facilitate Tn5supF-based sequencing of λ phage clones," Nuc. Acids Res., 19(22):6177-6182 (1991).	
	IW	Kunkel et al., "Rapid and efficient site-specific mutagenesis without phenotypic selection," Methods in Enzymology, 154:367-382 (1987).	
	ΙX	Kunkel, "Rapid and efficient site-specific mutagenesis without phenotypic selection", PNAS, 82: 488-493 (January 1985).	
	ΙΥ	Leung et al., "A Method For Random Mutagenesis of a Defined DNA Segment Using a Modified Polymerase Chain Reaction," <u>Techniques</u> , 1:11-15 (1989).	
	ız	Levichkin et al., "A New Approach to Construction of Hybrid Genes: Homolog Recombination Method", Mol. Biology, 29(5) part 1: 572-577 (1995).	
	JA	Lewis et al., "Efficient site directed in vitro mutagenesis using ampicillin selection", Nuc. Acids Res., 18(12): 3439-3443 (1990).	
	љ	Lorberbourn-Calski et al., "Cytotoxic activity of an interleukin 2-Pseudomonas exotoxin chimeric protein produced in Escherichia coli," PNAS, 85:1922-1926 (1988).	
	1C	Lowman, H.B. et al, "Affinity Maturation of Human Growth Hormone by Monovalent Phage Display," J. Mol. Biol., 234:564-578 (1993).	
	מנ	Majumder, K., "Ligation-free gene synthesis by PCR: synthesis and mutagenesis at multiple loci of a chimeric gene encoding OmpA signal peptide and hirudin," Gene, 110:89-94 (1992).	
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	JF	Marks et al., "By-Passing Immunization: Building High Affinity Human Antibodies by Chain Shuffling," Bio/Technology, 10:779-783 (1992).	
	1G	Marton et al., "DNA Nicking Favors PCR Recombination", Nucleic Acids Res., 19(9):2423-2426 (1991)	
$\overline{\mathbf{V}}$	JH	Maryon et al., "Characterization of recombination intermediates from DNA injected into Xenopus laevis occytes: evidence for a nonconservative mechnism of homologous recombination," Mol. Cell Biol., 11(6):3278-3287 (1991).	- N1

Examiner Signature	/Samuel Woolwine/	Date Considered	05/01/2007

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Substitute for	Substitute for form 1449B/PTO				Complete if Known
INFOR	BEATION	LDICO	COURT	Application Number	09/713,920 10/623036
	INFORMATION DISCLOSURE STATEMENT BY APPLICANT			Filing Date	Nevember 15, 2000 1/18/03
SIATE				First Named Inventor	Stemmer
		,		Art Unit	1048 /637
(us	(use as many sheets as necessary)			Examiner Name	Park, H. Samuel Wordwine
Sheet 12 of 17				Attorney Docket Number	-018097 032500US 0100. 227US

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Τ:
/S.W./	л	McCafferty et al., "Phage antibodies: filamentous phage displaying antibody variable domains," Nature, 348:552-554 (December 6, 1990).	
]]	Meyerhans et al., "DNA Recombination During PCR," Nucleic Acids Research, 18(7):1687-1691 (1990).	
	Ж	Michael, S.F., "Thermostable Ligase-Mediated Incorporation of Mutagenic Oligonucleotides During PCR Amplification," chapter 19 from Methods in Molecular Biology, PCR Cloning Protocols from Molecular Cloning to Genetic Engineering, eds. B. White, Humana Press, totowa, New Jersey, pages 189-195 (1997).	
	л	Moore et al., "Directed evolution of a para-nitrobenzyl esterase for aqueous-organic solvents", Nature Biotech., 14: 458-467 (April 1996).	
	ЛМ	Morl et al., "Group II intron RNA-catalyzed recombination of RNA in vitro," Nuc. Acids Res., 18(22):6545-6551 (1990).	
	JN	Mullis et al., "Specific Synthesis of DNA in Vitro via a Polymerase-Catalyzed Chain Reaction," Methods in Enzymology, 155:335-351 (1987).	
	JO	Mullis et al., "Specific Enzymatic Amplification of DNA In Vitro: The Polymerase Chain Reaction," Cold Spring Harbor Symposia on Quantitative Biology, 51:263-273 (1986).	
	JP	Near, "Gene Conversion Of Immunoglobulin Variable Regions In Mutagenesis Cassettes By Replacement PCR Mutagenesis", <u>Biotechniques</u> , 12(1):88-97 (1992)	
	1Q	Ner et al., "LABORATORY METHODS: A Simple and Efficient Procedure for Generating Random Point Mutations and for Codon Replacements Using Mixed Oligodeoxynucleotides," <u>DNA</u> , 7(2):127-134 (1988).	
	JR	Nissim et al., "Antibody fragments from a 'single pot' display library as immunochemical reagents," <u>EMBO Journal</u> , 13(3):692-698 (1994).	
	JS	Oliphant et al., "Cloning of Random-Sequence Oligodeoxynucleotides," Gene, 44(2-3):177-183 (1986).	
	JT	Olsen et al., "Hybrid Bacillus (1-3,1-4)-beta-glucanases: engineering thermostable enzymes by construction of hybrid genes," Mol. Gen. Genet., 225(2):177-185 (1991).	
	ĵŪ	Omura, "Philosophy of New Drug Discovery", Microbiol. Rev., 50(3): 259-279 (September 1986).	
V	1/\	Osuna et al., "Combinatorial mutagenesis of three major groove-contacting residues of <i>Eco</i> RI: single and double amino acid replacements retaining methyltransferase-sensitive activities," Gene, 106:7-12 (1991).	

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Examiner Signature	/Samuel Woolwine/	Date Considered	05/01/2007	

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Substitute for form 1449B/PTO				Complete if Known		
INFOR	BEATION	DICO	COURT	Application Number	99/713,920 10/6d3 036	
INFORMATION DISCLOSURE				Filing Date	-November-15, 2000 1/15/03	
STATE	STATEMENT BY APPLICANT			First Named Inventor	Stemmer	
				Art Unit	1648 /637	
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Sheet	13	of	17	Attorney Docket Number	-018097-032500US O100. 2 1 7US	

	<u>.</u>	OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
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/S.W./	1W	Paabo et al., "DNA Damage Promotes Jumping between Templates during Enzymatic Amplification," <u>J. Biol. Chem.</u> , 265(8):4718-4721 (March 15, 1990).	
	ıχ	Perlak, "Single Step Large Scale Site-Directed In Vitro Mutagenesis Using Multiple Oligonucleotides", Nucleic Acids Res., 18(24):7457-7458 (1990)	
	ΊΥ	Pharmacia Catalog, pp. 70-71 (1993 Edition).	
	JZ	Piepersberg, "Pathway Engineering in Secondary Metabolite-Producing Actinomycetes", Crit. Rev. Biotech., 14(3):251-285 (1994).	
	KA	Pompon et al., "Protein Engineering by cDNA Recombination in Yeasts: Shuffling of Mammalian Cytochrome P-450 Functions," Gene, 83(1):15-24 (1989).	
	KB	Prasher, "Using GFP to see the light", TIG, 11(8) (August 1995).	
	KC	Prodromou et al., "PROTOCOL, Recursive PCR: a novel technique for total gene synthesis," Protein Engineering, 5(8):827-829 (1992).	
	KD	Rao et al., "Recombination and Polymerase Error Facilitate Restoration of Infectivity in Brome Mosaic Virus," <u>Journal of Virology</u> , 67(2):969-979 (1993).	
	KE	Rapley, "Enhancing PCR Amplification And Sequencing Using DNA-Binding Proteins", Mol. Biotechnol., 2(3):295-298 (1994)	
	KF	Reidhaar-Olson et al., "Combinatorial Cassette Mutagenesis as a Probe of the Informational Content of Protein Sequences," Science, 241:53-57 (1988).	
	KG	Rice et al., "Random PCR mutagenesis screening of secreted proteins by direct expression in mammalian cells", PNAS, 89: 5467-5471 (June 1992).	
	КН	Robles et al., "Hydropathy and Molar Volume Constraints on Combinatorial mutants of the Photosynthetic Reaction Center," J. Mol. Biol., 232:242-252 (1993).	
	кі	Rouwendal et al., "Simultaneous Mutagenesis of Multiple Sites: Application of the Ligase Chain Reaction Using PCR Products Instead of Oligonucleotides," <u>BoiTechniques</u> , 15(1):68-70, 72-74, 76 (1993).	
$\sqrt{}$	ĸJ	Saiki et al., "Diagnosis of sickle Cell Anemia and β-Thalassernia with Enzymatically Amplified DNA and Nonradioactive Allele-Specific Oligonucleotide Probes," New England J. of Medicine, 319(9):537-541 (September 1, 1988).	

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Sheet 14 of 17				Attorney Docket Number	-018007-032500USONO.227US		

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
/S.W./	KK	Saiki et al., "analysis of enzymatically amplified β-globin and HLA-DQα DNA with allele-specific oligonucleotide probes," Nature, 324:163-166 (November 13, 1986).	
	KL.	Saiki et al., "Enzymatic Amplification of β-Globin Genomic Sequences and Restriction Site analysis for Diagnosis of Sickle Cell Anemia," Science, 230:1350-1354 (December 20, 1985).	
	КМ	Saiki et al., "Primer-Directed Enzymatic Amplification of DNA with a Thermostabl; e DNA Polymerase," Science, 239:487-491 (January 20, 1988).	
	KN	Sambrook et al., Molecular Cloning, A Laboratory Manual, Cold Spring Laboratory Press, Cold Spring Harbor, New York (1989).	
	ко	Sambrook et al., <i>Molecular Cloning: A Laboratory Manual</i> , 2nd edition, Cold Spring Harbor Laboratory Press, pages 14.2, 14.34, and 14.35 (1989).	
	КР	Sandhu et al., "Dual Asymmetric PCR: One-Step Construction of Synthetic Genes," <u>BioTechniques</u> , 12(1):14-16 (1992).	
	КQ	Scharf et al., "Direct Cloning and Sequence Analysis of Enzymatically Amplified Genomic Sequences," Science , 233:1076-1078 (September 1986).	
	KR	Scott et al., "Searching for Peptide Ligands with an Epitope Library," Science, 249:386-390 (July 20, 1990).	
	KS	Shao et al., "Random-priming in vitro recombination: an effective tool for directed evolution," Nuc. Acids Res., 26(2):681-683 (1998).	
	кт	Shi et al., "Rapid PCR Construction of a Gene Containing Lym-1 Antibody Variable Regions," PCR Methods and Applications, 3:46-53 (1993).	
	KU	Shuldiner et al., "Hybrid DNA artifact from PCR of closely related target sequences," Nuc. Acids Res., 17(11):4409 (1989).	
	к٧	Sikorski et al., "In Vitro Mutagenesis and Planned Shuffling: From Cloned Gene to Mutant Yeast," Methods in Enzymology, 194:302-318 (1991).	
	ĸw	Simpson et al., "Two paradigms of metabolic engineering applied to amino acid biosynthesis", <u>Biochem. Soc. Transactions</u> , vol. 23 (1995).	
V	кх	Smith et al., "Unwanted Mutations in PCR Mutagenesis: Avoiding the Predictable," PCR Methods and Applications, 2(3):253-257 (February 1993).	

Examiner Date /Samuel Woolwine/ 05/01/2007 Signature Considered



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Substitute for	form 1449B/PT	·o		Complete if Known			
INFOR	AATION	DICOL	COUDE	Application Number	09/713,920 10/623036		
			OSURE	Filing Date	Nevember 15, 2000 1//-9 /03		
STATE	MENTE	BY APP	LICANT	First Named Inventor	Stemmer		
		•		Art Unit	1648 /637		
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Sheet	15	of	17	Attorney Docket Number	018007-032500US-0100. 427US		

	·	OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examiner Cite No.1		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T2
/S.W./	кү	Smith et al., "Localized sex in bacteria," Nature, 349:29-31 (1991).	
	KZ	Steele et al., "Techniques for Selection of Industrially Important Microorganisms", Ann. Rev. Microbiol., 45: 89-106 (1991).	
	LA	Stemmer, "Rapid Evolution of a Protein in Vitro by DNA Shuffling," Nature, 370:389-391 (1994).	
	LB	Stemmer, "DNA Shuffling by Random Fragmentation and Reassembly: In Vitro Recombination for Molecular Evolution" Proc. Natl. Acad. Sci. USA , 91(22):10747-10751 (1994).	
	rc	Stemmer et al., "Selection of an Active Single Chain FV Antibody from a Protein Linker Library Prepared by Enzymatic Inverse PCR," <u>Biotechniques</u> , 14(2):256-265 (1992).	
	LD	Stemmer, "Searching Sequence Space", Biotechnology, 13:549-553 (1995)	
	LE	Stemmer et al., "Single-Step Assembly Of A Gene And Entire Plasmid From Large Numbers Of Oligodeoxyribonucleotides", Gene, 164(1):49-53 (1995)	
	LF	Stemmer, "The Evolution of Molecular Computation", Science, 270(5241):1510 (1995)	
	LG	Stemmer, "Sexual PCR and Assembly PCR" Encyclopedia Mol. Biol., VCH Publishers, New York, pp. 447-457 (1996)	
	LH	Stemmer et al., "Increased Antibody Expression from Escherichia-Coli Through Wobble-Base Library Muatagenesis by Enzymatic Inverse PCR," Gene, 123(1):1-7 (1993).	
	LI	Stemmer et al., "Enzymatic Inverse PCR – A Restriction Site Independent, single-Fragment Method for High-Efficiency, Site-Directed Mutagenesis," <u>Biotechniques</u> , 13(2):214 (1992).	
	n	Stemmer et al., "Expression of Antibody FV Fragments Specific for a Heavy Metal Chelate Indium Edta In Escherichia-Coli," J. Cell Biochem., Suppl. 0(15 part G), pg. 217 (1991).	
	LK	Stemmer et al., "A 20-Minute Ethidium Bromide High-slat Extraction Protocol for Plasmid DNA," <u>Biotechniques</u> , 10(6):726 (1991).	
Ψ	LL	Stephanopoulos et al., "Metabolic engineering - methodologies and future prospects", <u>Trends Biotech.</u> 11: 392-396 (1993).	

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Examiner Signature	/Samuel Woolwine/	Date Considered	05/01/2007

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Substitute t	for form 1449B/PT(0	•		Complete if Known
INFO	INFORMATION DISCLOSURE STATEMENT BY APPLICANT			Application Number	09/713,920- 10/623036
				Filing Date	November 15, 2000 ///8/03
SIAI	EMENT B	Y AP	PLICANT	First Named Inventor	Stemmer
				Art Unit	1 648 /637
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Sheet	16	of	17	Attorney Docket Number	018007-032500US 0/00 227/15/

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Examiner Initials * Cite No.1 /S.W./ LM		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	т;
		Stephanopoulos, "Metabolic engineering", Curr. Opin. Biotech., 5: 196-200 (1994).	
	LN	Villarreal et al., "A General Method of Polymerase-Chain-Reaction-Enabled Protein Domain Mutagenesis: Construction of a Human Protein S-Osteonectin Gene," <u>Analytical Biochem.</u> , 197:362-367 (1991).	
	ro	Wang et al., "Identification Of Glial Filament Protein And Vimentin In The Same Intermediate Filament System In Human Glioma Cells", Proc. Natl. Acad. Sci. USA, 81(7):2102-2106 (1984)	
	LP	Weber et al., "Formation of Genes Coding for Hybrid Proteins by Recombination Between Related, Cloned Genes in E. Coli," Nucleic Acids Research, 11(16):5661-5669 (1983)	
	LQ	Wehmeier, "New multifunctional Escherichia coli-Streptomyces shuttle vectors allowing blue-white screening on XGal plates", Gene, 165: 149-150 (1995).	
	LR	Weissenhorn et al., "Chimerization of antibodies by isolation of rearranged genomic variable regions by the polymerase chain reaction," Gene, 106:273-277 (1991).	
	LS	Winter et al., "Making Antibodies By Phage Display Technology", Ann. Rev. Immunol., 12:433-455 (1994)	
	LT	Wu et al., "Allele-specific enzymatic amplification of beta-globin fgenomic for diagnosis of sickle cell anemia," PNAS, 86(6):2757-2760 (1989).	
	LU	Yao et al., "Site-directed Mutagenesis of Herpesvirus Glycoprotein Phosphorylation Sites by Recombination Polymerase Chain Reaction," PCR Methods and Applications, 1(3):205-207 (February 1992).	
	LV	Yolov et al., "Constructing DNA by polymerase recombination," Nuc. Acids Res., 18(13):3983-3986 (1990).	
	LW	Yon et al., "Precise gene fusion by PCR," Nuc. Acids Res., 17(12):4895 (1989).	
	LX	Youvan et al., "Recursive Ensemble Mutagenesis: A Combinatorial Optimization Technique for Protein Engineering," from Parallel Problem Solving from Nature, 2, Manner eds., pp. 401-410 (1992).	
	LY	Zhang et al., "Directed Evolution Of A Fucosidase From A Galactosidase By DNA Shuffling And Screening", Proc. Natl. Acad. Sci. USA, 94(9):4504-4509 (1997)	
V	LZ	Zhao et al., "Molecular Evolution by Staggered Extension Process (StEP) In Vitro Recombination", Nature Biotech., 16:258-261 (1998)	

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Park, H. (

Substitute for form 1449B/PTO Complete if Known **Application Number** 00/713,920 10/623036 INFORMATION DISCLOSURE Filing Date November 15, 2000 7/18/03 STATEMENT BY APPLICANT **First Named Inventor** Stemmer Art Unit (use as many sheets as necessary) -

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/S.W./	MA	Zoller et al., "Oligonucleotide-directed mutagenesis: a simple method using two oligonucleotide primers and a single-stranded DNA template," Methods in Enzymology, 154:329-350 (1987).			
	МВ	Zoller, M.J., "New recombinant DNA methodology for protein engineering," <u>Curr. Opin, Biotech.</u> , 3:348-354 (1992).			
	мс	Biotransformations, Pathogenesis, and Evolving Biotechnology, Program and Absracts, Pseudomonas '89, American Society for Microbiology and The University of Illinois, 7/9-13/89, abstracts 11-21 to 11-25.			
	MD	Statutory Declaration of Mae Li Gan in Australian Opposition against application 703264. September 22, 2000			
<u> </u>	ME	Statutory Declaration of Dr. Gerald Joyce in Australian Opposition against application 703264. December 21, 2000			
	MF	Statutory Declaration of Ngarie Petit-Young in Australian Opposition against application 703264. September 20, 2000			
	MG	Statutory Declaration of Ruth Bird in Australian Opposition against application 703264. September 20, 2000			
	МН	Request for leave to amend the Statement of Grounds and Particulars re: opposition 703264 in Australia (1/25/01).			
	MI	Amended Statement of Particulars re: opposition 703264 in Australia (1/25/01).			
V	МЈ	Opposition Statement in matter of Australian Patent Application 703264 (Affymax Technologies NV), filed by Diversa Corporation on September 23, 1999.			
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	Application Number		10623036	
INFORMATION DIOCHOCKE	Filing Date		2003-07-18	
INFORMATION DISCLOSURE	First Named Inventor	Willen	n P.C. Stemmer	
STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Art Unit		1637	
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Application Number		10623036
Filing Date		2003-07-18
First Named Inventor	Willer	n P.C. Stemmer
Art Unit		1637
Examiner Name	Samu	el C. Woolwine
Attorney Docket Number		0100.227US

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/S.W./	.W./ 8 Stahl, S. et al., "Solid-phase gene assembly of constructs derived from the plasmodium falciparum malaria blood-stage antigen Ag332," BioTechniques14(3):424-434) (1993)								
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